



# Study toward the convergent total synthesis of the aporphine alkaloid PO-3

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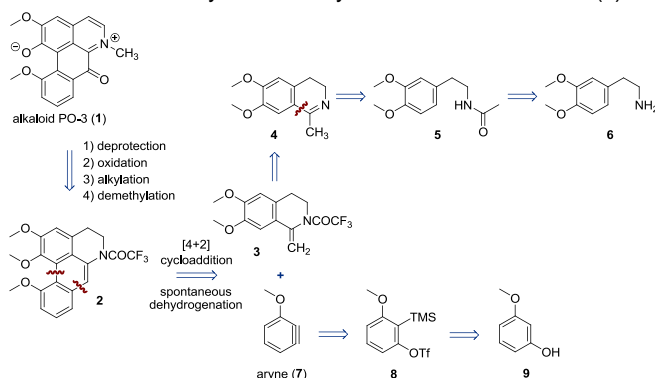
## INTRODUCTION

Due to the great importance of benzyne as a highly reactive intermediate in organic chemistry, with applications in total syntheses<sup>1</sup> and in preparations of functional materials,<sup>2</sup> we intend to accomplish the convergent total synthesis of the aporphine alkaloid PO-3 (**1**), a natural dye of green color,<sup>3</sup> employing as key reaction a [4+2] cycloaddition between 1-methylene-1,2,3,4-tetrahydroisoquinoline (**3**) and the benzyne derivative **7**, formed from 2-(trimethylsilyl)aryl triflate (**8**), under mild reaction conditions.

## RESULTS AND DISCUSSION

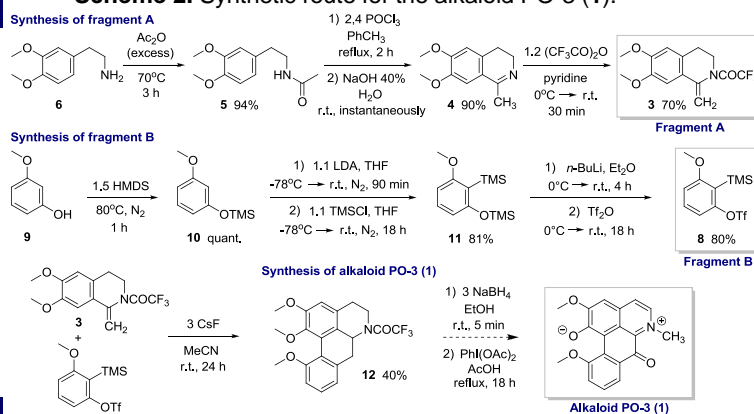
Attracted by the dye property of the aporphine alkaloid PO-3 (**1**),<sup>3</sup> we decide to perform the total synthesis of the mentioned natural product of green color, employing a convergent synthetic route. Thus, according to the retrosynthetic analysis, the alkaloid PO-3 (**1**) can be obtained by functional group transformations from the intermediate **2**, which can be produced by the [4+2] cycloaddition reaction between 1-methylene-1,2,3,4-tetrahydroisoquinoline (**3**) and 2-(trimethylsilyl)aryl triflate (**8**), followed by a spontaneous dehydrogenation process<sup>3</sup> (Scheme 1).

Scheme 1. Retrosynthetic analysis for the alkaloid PO-3 (**1**).



Guided by the retrosynthetic analysis outlined in Scheme 1, we started the synthesis to obtain the dye PO-3 (**1**), by the preparations of 1-methylene-1,2,3,4-tetrahydroisoquinoline (**3**) (fragment A) and of the silylaryl triflate **8** (fragment B), which were obtained in good yields (Scheme 2).

Scheme 2. Synthetic route for the alkaloid PO-3 (**1**).



Afterwards, compound **3** was subjected to the [4+2] cycloaddition reaction with the aryne precursor **8**, resulting in the highly regioselective formation of the intermediate **12** in 40% yield, which contains the basic structure of the alkaloid PO-3 (**1**). However, for our surprise, the process of spontaneous dehydrogenation did not occur.<sup>3</sup> After optimizing the reaction which leads to the intermediate **12**, we intend to obtain the alkaloid PO-3 (**1**) by reactions described in the literature<sup>3,4</sup> (Scheme 2).

## CONCLUSION

Fragments A and B were obtained by reactions that presented high yields. Compounds **3** and **8** are going to be used in the optimization of the [4+2] cycloaddition reaction, i.e., the key step for the convergent synthesis of the aporphine alkaloid PO-3 (**1**).

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